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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/196,673	11/20/98	MCCAFFERTY	J 28111/32106B

DAVID W CLOUGH
MARSHALL O'TOOLE GERSTEIN MURRAY & BORUN
6300 SEARS TOWER
233 SOUTH WACKER DRIVE
CHICAGO IL 60606-6402

HM12/0411

EXAMINER

PONNALURI, P

ART UNIT

PAPER NUMBER

1627

8

DATE MAILED:

04/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/196,673

Applicant(s)
McCafferty et al

Examiner
P. Ponnaluri

Group Art Unit
1627



☒ Responsive to communication(s) filed on Jan 21, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 44-144 is/are pending in the application.

Of the above, claim(s) 66-77 and 110-144 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 44-65 and 78-109 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☒ received in Application No. (Series Code/Serial Number) 07/971,857.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7

☒ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

1. This application is a continuation of application serial number 07/971,857, which is a 371 of PCT/GB91/01134.
2. Claims 44-144 are currently pending in this application.
3. The preliminary amendment A, filed on 11/20/98 (cancels claims 1-43), and the preliminary amendment B, filed on 11/20/98 (adds new claims 44-144) and amendment C filed on 1/21/00, have been fully considered and entered into the application.

Election/Restriction

4. Applicant's election with traverse of group 1, claims 44-65, in Paper No. 6 is acknowledged. The traversal is on the ground(s) that groups 1, 5 and 6 inventions are drawn to methods of obtaining specific binding pair members, which are closely related. Applicants arguments are persuasive because, the newly amended independent claims 78, 80, 82 and 84 (group 5 inventions) recite that the specific binding pair member comprises an enzyme or a fragment of thereof, and is at least 100 amino acids (claims 78 and 80) or at least 200 amino acids (claims 82 and 84), thus the groups 5 and 6 inventions are drawn to the same subject matter of elected group 1. Groups 1, 5 and 6 (claims 44-65 and 78-109) are examined together in this application.
5. Claims 66-77, 110-144 are withdrawn from further consideration by the examiner, 37

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CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

6. Claims 44-65 and 78-109 are currently being examined in this application.

Priority

7. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies have been filed in parent Application No. 07/971,857.

Drawings

8. The substitute drawings received on 11/20/98 (preliminary amendment A) have been fully considered.
9. The drawings filed on 11/20/98 were objected by the draftsman (see PTO 948). Applicant is invited to notice that boxes 5-6 and 12 in PTO 948 were checked by the draftsman. Applicant is encouraged to amend the specification so that the description of renumbered figure corresponds to the renumbered figures.

Specification

10. Applicants are requested to update the current status of parent application 08/244,597, in the specification page 1.
11. Applicants are requested to delete blank space in specification page 111.
12. The use of the trademarks TITERTEK (in page 100, line 16), SIGMA (in page 103, line

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14), SEPHAROSE (page 109, lines 3 and 4) have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 U.S.C § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 44-65 and 78-109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 is vague and indefinite by reciting '.....encoding a genetically diverse population of polypeptides provided by mutating nucleic acid encoding a specific binding pair member which comprises an enzyme or a fragment thereof...', it is not clear what does applicant mean provided by mutating nucleic acid. It is not clear whether the genetically diverse population of polypeptides

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are provided by mutating nucleic acid or the library of nucleic acid sequences are provided by mutating nucleic acid. For compact prosecution the claim is interpreted as 'a library of nucleic acid sequences encoding a genetically diverse population of polypeptides, said library of nucleic acid sequences are provided by mutating nucleic acid encoding said specific binding pair member, and said specific binding pair member comprises an enzyme or fragment thereof'. Claim 44 is vague and indefinite by reciting '...wherein polypeptides encoded within the library are each expressed as a fusion with a coat protein..' it is not clear what does applicant mean by polypeptides encoded within the library. If applicant mean that the polypeptides encoded by the library of nucleic acid sequences, applicant are requested to amend the claim as "...wherein said polypeptides with a coat protein surface component of a filamentous bacteriophage are expressed as a fusion protein, and said bacteriophage particle displays the fusion protein at the surface, ..". Applicants are suggested to replace 'a said fusion' with "said fusion".

Claim 44 recites the limitation "the genetic material" in line 11. There is insufficient antecedent basis for this limitation in the claim. Claim 44 recites the limitation "said particle" in line 12. There is insufficient antecedent basis for this limitation in the claim. Applicants are suggested to amend the claim as "whereby genetic material of each said bacteriophage particles includes a nucleic acid sequence encoding the polypeptide."

Claims 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to obtain a member of specific binding pair. The

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independent claim recites a method of obtaining a member of specific binding pair, and the method comprises: expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides. However, the claimed method is incomplete, because the claim does not say how the specific binding pair is obtained from the phage particles. The claim does not include method steps in which the recombinant host cells are screened or selected for phage particles displaying the specific binding pair, and obtaining nucleic acid encoding the specific binding pair from the selected phage particles. The claims lack steps in which the host cells expressing the specific binding pair are selected by affinity selection in presence of a ligand.

Claims 46-47 recite the limitation "the gene III capsid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 48 is vague and indefinite by reciting '...an individual displayed polypeptide specific binding pair member or a mixed population of displayed polypeptide specific binding pair members associated in respective particles with nucleic acid...', it is not clear whether applicant mean phage particle or specific binding pair member associated in respective particles. If applicants mean that the phage particle displaying the polypeptide, applicants are suggested to amend the claim as "an individual phage particle displaying the polypeptide...". Claim 48 is indefinite by reciting 'a mixed population of displayed polypeptide specific binding pair members', it is not clear what does applicant mean by mixed population of displayed polypeptide. Does applicant mean mixed population of phage displaying polypeptides or mixed population of

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polypeptides displayed on the phage? It is confusing, because claim 44 recites that the at the surface of the phage the polypeptide is displayed. Applicants are requested to clarify.

Claim 48 is indefinite by reciting 'the specific binding pair member or members thus provided having ability to bind a complementary ligand'. Applicants are suggested to amend the claim as "the specific binding pair member or the specific binding pair members bind to a complementary ligand."

Claim 53 is vague and indefinite by reciting 'wherein the particles are selected by enzymatic activity', applicants are requested to clarify what does it mean by selected by enzymatic activity. It is not clear whether the particles have enzymatic activity or the polypeptides displayed on the phage have enzymatic activity. If applicant mean that the polypeptides displayed on the phage particles have enzymatic activity, applicants are suggested to amend the claim.

Claims 55 and 57 are vague by reciting in step (ii), producing from nucleic acid obtained in step (I) nucleic acid which encodes a specific binding pair member. It is not clear what does applicant mean by producing nucleic acid from the nucleic acid obtained in step I), because the nucleic acid obtained in step I), is the nucleic acid which encodes the member of specific binding pair. Does applicant mean that the affinity purification or selection of phage particles that display the specific binding pair member is repeated, it is not clear. Applicants are requested to clarify. Applicants are suggested in claims 55, 57 replace 'a said derivative specific binding pair member' with "said derivative specific binding pair member".

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Claims 60-65 are vague and indefinite by reciting in step (ii) ‘ nucleic acid which encodes a derivative specific binding pair member..’, it is not clear what does applicant mean by derivative specific binding pair member. It is not clear whether the derivative specific binding pair member has similar properties as the specific binding pair member and does it bind specifically to the ligand of interest. The deletions, substitution or insertions of amino acids might change the binding characteristics of the specific binding pair member. It is also not clear what does applicant mean by the linkage of another molecule, what is the another molecule. Is it another peptide which might alter the peptide which is encoded by the nucleic acid obtained in step (I) or a marker. Applicants are requested to clarify what is the derivative of specific binding pair member.

Applicants are suggested in claims 61, 63, and 65 replace ‘a said derivative specific binding pair member’ with “said derivative specific binding pair member”.

Claims 78-85 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to obtain a specific binding pair member from the particle displaying the specific binding pair member. The instant claims are drawn to a method of obtaining a member of a specific binding pair, by contacting a library of filamentous bacteriophage particles with a desired ligand and separating particles displaying a specific binding pair members which bind to said desired ligand. However, the claimed method fails to teach how to get the specific binding pair member displayed by the particle . Applicants are suggested to include all the method steps.

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Claims 78, 80, and 82 are vague and indefinite by reciting ‘..a polypeptide which is a specific binding pair member with ability to bind a complementary ligand..’, applicants are suggested to amend the claims as “...said member of specific binding pair binds to a complementary ligand...” The claim are vague and indefinite by reciting ‘said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least ... amino acids..’, it is not clear what does applicant mean by said nucleic acid including a sequence encoding said polypeptide provided by mutation. It is not clear whether applicant mean that the nucleic acid encoding the fusion is provided by mutation of the nucleic acid encoding a specific binding pair member or the nucleic acid encoding the polypeptide which is a specific binding pair member is provided by mutation. Applicants are suggested to clarify. It is not clear in line 10, whether applicants are referring to the same specific binding pair member (line 7) or the specific binding pair is different. Applicants are suggested to amend the claim as “...the particles contain nucleic acid encoding said fusion, said nucleic acid includes a sequence encoding the polypeptide, and nucleic acid sequence encoding the polypeptide is provided by mutation of nucleic acid encoding said specific binding pair member, and said specific binding pair member comprises an enzyme or fragment thereof, and said enzyme or fragment thereof is at least ... amino acids and binds said desired ligand..”

Claims 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, and 101 recite the limitation "the gene III capsid of phage fd" in line 2. There is insufficient antecedent basis for this limitation in the

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claims. Applicants are suggested to amend the claims as “wherein said coat protein surface component is gene III capsid protein of phage fd..”.

Claims 94-101 are vague by reciting in step (ii), producing from nucleic acid obtained in step (I) nucleic acid which encodes a specific binding pair member. It is not clear what does applicant mean by producing nucleic acid from the nucleic acid obtained in step I), because the nucleic acid obtained in step I), is the nucleic acid which encodes the member of specific binding pair. Does applicant mean that the affinity purification or selection of phage particles that display the specific binding pair member is repeated, it is not clear. Applicants are requested to clarify.

Claims 102-109 are vague and indefinite by reciting ‘ nucleic acid which encodes a derivative specific binding pair member..’, it is not clear what does applicant mean by derivative specific binding pair member. It is not clear whether the derivative specific binding pair member has similar properties as the specific binding pair member and does it bind specifically to the ligand of interest. The deletions, substitution or insertions of amino acids might change the binding characteristics of the specific binding pair member. It is also not clear what does applicant mean by the linkage of another molecule, what is the another molecule. Is it another peptide which might alter the peptide which is encoded by the nucleic acid obtained in step (I) or a marker. Applicants are requested to clarify what is the derivative of specific binding pair member. Claims 103, 105, 107 and 109 are vague and indefinite by reciting ‘producing by expression from encoding nucleic acid obtained by a method according to claim ..a said derivative specific binding pair member.’, It is not clear what does applicant mean by producing by expression from encoding

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nucleic acid. Does applicant mean that the producing by expression of the nucleic acid obtained in the method of claim ..step (I). Applicants are suggested to amend the claims. Applicants are suggested in claims 103, 105, 107 and 109 replace 'a said derivative specific binding pair member' with "said derivative specific binding pair member".

Claim Rejections - 35 U.S.C § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

17. Claims 44, 46, 48-49, 78-81, 86-89 and 94-97 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,427,908 (Dower et al)(102 (e) reference, because of filing date May 1, 1990).

The claims are drawn to a method of obtaining a specific binding pair member, the specific binding pair member comprises an enzyme or fragment thereof which is 100-200 amino acids, and the method comprises by expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides provided by mutating nucleic acid encoding the specific binding pair member, and the polypeptides are displayed on the surface of a filamentous phage particles , and selecting the phage particles that display the polypeptide (which

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is enzyme or fragment thereof) which bind to the desired ligand, and obtaining the specific binding pair member from the nucleic acid of the selected phage.

Dower et al teach a method for screening a DNA library for a nucleotide sequence which encodes a protein of interest, and the protein of interest of the invention is an antibody or fragment thereof (Fab) or proteins such as hormones, enzymes, interferons or zymogen (see column 3, lines 19-25) which has a desired binding specificity. Dower et al teach when the desired protein is an immunoglobulin, a library expressing antibody light chain binding regions is combined with a library expressing antibody heavy chain regions, thereby constructing combinatorial Fab expression libraries (see column 4, lines 65-68, column 5, line 1). The reference teaches that the method comprises the following steps: expressing in a recombinant host organism a first polypeptide chain of a specific binding pair fused to a component of a secreted replicable genetic display package that displays the polypeptide at the surface of the package and expressing in a recombinant organism a second polypeptide chain of said multimer and allowing the polypeptide chains to come together to form a multimer (see column 2, lines 51-59). Dower et al teach that the preferred vectors are filamentous phage fd, f1, and M13 (see column 2, lines 47-48). The reference teaches expression of nucleic acid of each polypeptide chain that is capable of being packaged as replicable genetic display package (see columns 1-2). The reference teaches a method to obtain nucleic acid encoding at least one of said first and second polypeptide chains from a library of nucleic acids encoding said chain (see column 12, lines 49-50). Dower et al teach fusion with pIII coat protein (capsid protein) thus the fusion with the capsid protein is displayed

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on the phage coat protein while the non-fused protein is expressed in wild type form. The reference teaches that a DNA library is constructed by cloning cDNA (vH region) from the donor cells into a coat protein gene (gene III) cloning site, and the cloning sequences (vH domains) are ultimately expressed as polypeptides up to 120 amino acids (refers to the specific binding pair member comprises an enzyme or fragment thereof and is at least 100 amino acids of the instant claims). The reference teaches although a large peptide fragment near the N-terminus of the coat protein may cause a decrease in phage infectivity and/or yield compared to phage with smaller, but the larger fragments may still be effectively enriched by subsequent rounds of panning (see column 8). The reference teaches that the host cells are then infected with the phage and cultivated under conditions allowing for expression and assembly of phage particles, and the appropriate host cells for bacteriophage are various strains of E.coli (see column 6, lines 23-25). The reference method teaches to isolate phage which contain cloned library sequences which encode a desired protein and thus to ultimately isolate the nucleic acid sequences, phage harvested from the bacteria are affinity purified (see column 6, lines 54-58). Dower et al teach that the phage identified having an antibody recognized by the target are selected and DNA prepared and sequenced by standard methods to determine DNA and amino acid sequence of the particular antibody, and the DNA may be recloned in a suitable eukaryotic or prokaryotic expression vector and transfected into an appropriate host for production of large amounts of protein (see column 12).

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Dower et al teach that the disclosed method of screening a DNA library for nucleotide sequence which encodes a protein of interest is typically an antibody or fragment thereof, but may also be any protein which may be cloned from a nucleotide library, and such proteins include, for example, hormones, interferons, interleukins and enzymes (see column 3, lines 18-24, in particular). Dower et al teach antibodies with catalytic activities (refers to enzymatic activity of the instant claims) may be enriched in groups of antibodies with high affinity for reactants but low affinity for products. A double screen to enrich for antibodies with these characteristics is useful in finding antibodies to catalyze reactions, and catalytic antibodies (refer to enzyme of the instant claims) capable of certain cleavage reactions may be selected using the disclosed method. For example a catalytic antibodies (refer to enzymes of the instant claims) capable of cleavage a specific amino acid from the end of a peptide (refers to desired ligand of instant claims) may be selected by immobilizing the peptide and panning the antibody library under conditions to promote binding but not cleavage and followed by wash, this allows antibodies that recognized the end group to bind and become immobilized, and to separate the antibodies capable of cleavage, the conditions are shifted in favor of cleavage, which would release the antibody-phage capable of cleavage from the immobilized peptide (see column 11, lines 29-51, in particular).

Dower et al teach that the method can be applied in therapeutic, diagnostic applications, and in preparation of catalytic antibodies. Dower et al teach that the disclosed method facilitate the screening process, thereby enabling DNA sequences which encode protein of interest, and particularly antibody molecules to be recloned and expressed, and these procedures may be used

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to obtain an antibody to a preselected target molecule, thus, the difficulties and labor intensive process of generating monoclonal antibodies may be avoided. The reference clearly anticipates the claimed invention.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 44-65 and 78-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,427,908 (Dower et al).

Dower et al teach a method for screening a DNA library for a nucleotide sequence which encodes a protein of interest, and the protein of interest of the invention is an antibody or fragment thereof (Fab) or proteins such as hormones, enzymes, interferons or zymogen (see column 3, lines 19-25) which has a desired binding specificity. Dower et al teach when the

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desired protein is an immunoglobulin, a library expressing antibody light chain binding regions is combined with a library expressing antibody heavy chain regions, thereby constructing combinatorial Fab expression libraries (see column 4, lines 65-68, column 5, line 1). The reference teaches that the method comprises the following steps: expressing in a recombinant host organism a first polypeptide chain of a specific binding pair fused to a component of a secreted replicable genetic display package that displays the polypeptide at the surface of the package and expressing in a recombinant organism a second polypeptide chain of said multimer and allowing the polypeptide chains to come together to form a multimer (see column 2, lines 51-59). Dower et al teach that the preferred vectors are filamentous phage fd, f1, and M13 (see column 2, lines 47-48). The reference teaches expression of nucleic acid of each polypeptide chain that is capable of being packaged as replicable genetic display package (see columns 1-2). The reference teaches a method to obtain nucleic acid encoding at least one of said first and second polypeptide chains from a library of nucleic acids encoding said chain (see column 12, lines 49-50). Dower et al teach fusion with pIII coat protein (capsid protein) thus the fusion with the capsid protein is displayed on the phage coat protein while the non-fused protein is expressed in wild type form. The reference teaches that a DNA library is constructed by cloning cDNA (vH region) from the donor cells into a coat protein gene (gene III) cloning site, and the cloning sequences (vH domains) are ultimately expressed as polypeptides up to 120 amino acids (refers to the specific binding pair member is at least 100 amino acids of the instant claims). The reference teaches although a large peptide fragment near the N-terminus of the coat protein may cause a decrease in phage

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infectivity and/or yield compared to phage with smaller, but the larger fragments may still be effectively enriched by subsequent rounds of panning (see column 8). The reference teaches that the host cells are then infected with the phage and cultivated under conditions allowing for expression and assembly of phage particles, and the appropriate host cells for bacteriophage are various strains of E.coli (see column 6, lines 23-25). The reference method teaches to isolate phage which contain cloned library sequences which encode a desired protein and thus to ultimately isolate the nucleic acid sequences, phage harvested from the bacteria are affinity purified (see column 6, lines 54-58). Dower et al teach that the phage identified having an antibody recognized by the target are selected and DNA prepared and sequenced by standard methods to determine DNA and amino acid sequence of the particular antibody, and the DNA may be recloned in a suitable eukaryotic or prokaryotic expression vector and transfected into an appropriate host for production of large amounts of protein (see column 12).

Dower et al teach that the disclosed method of screening a DNA library for nucleotide sequence which encodes a protein of interest is typically an antibody or fragment thereof, but may also be any protein which may be cloned from a nucleotide library, and such proteins include, for example, hormones, interferons, interleukins and enzymes (see column 3, lines 18-24, in particular). Dower et al teach antibodies with catalytic activities (refers to enzymatic activity of the instant claims) may be enriched in groups of antibodies with high affinity for reactants but low affinity for products. A double screen to enrich for antibodies with these characteristics is useful in finding antibodies to catalyze reactions, and catalytic antibodies (refer to enzyme of the instant

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claims) capable of certain cleavage reactions may be selected using the disclosed method. For example a catalytic antibodies (refer to enzymes of the instant claims) capable of cleavage a specific amino acid from the end of a peptide (refers to desired ligand of instant claims) may be selected by immobilizing the peptide and panning the antibody library under conditions to promote binding but not cleavage and followed by wash, this allows antibodies that recognized the end group to bind and become immobilized, and to separate the antibodies capable of cleavage, the conditions are shifted in favor of cleavage, which would release the antibody-phage capable of cleavage from the immobilized peptide (see column 11, lines 29-51, in particular).

Dower et al teach that the method can be applied in therapeutic, diagnostic applications, and in preparation of catalytic antibodies. Dower et al teach that the disclosed method facilitate the screening process, thereby enabling DNA sequences which encode protein of interest, and particularly antibody molecules to be recloned and expressed, and these procedures may be used to obtain an antibody to a preselected target molecule, thus, the difficulties and labor intensive process of generating monoclonal antibodies may be avoided.

The claimed invention differs from the prior art teachings by reciting that the specific binding pair is enzyme or fragment thereof is at least 200 amino acids. Dower et al do not specifically teach that the specific binding pair is 200 amino acids. However, Dower et al teach when the desired protein is a multichain protein, such as an antibody or binding fragment thereof (Fab), the chains (vH or vL) are cloned as separate libraries in a different plasmid vectors, amplified, and subsequently the fragments (vL fragments) are installed into the first chain-coat

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protein library vector (first chain-coat protein is an vH or fragment thereof which encodes a polypeptide of 120 amino acids), thus randomly combining vH and vL sequences in a single phage genome (vH and vL together would become more than 200 amino acids), and the number of possible combinations of heavy and light chains probably exceed 10^{12} (see column 9). Thus, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the method of screening a DNA library for nucleotide sequence which encodes a protein of interest taught by Dower et al to identify an enzyme or fragment which is 200 amino acids, because Dower et al teach catalytic antibodies (refers to enzymes of the instant claims) which are capable of cleavage(refers to desired enzymatic activity of the instant claims) and the reference teaches that vH domains (of antibodies) are expressed as polypeptides of about 120 amino acids, and when the desired protein is a multichain protein the reference teaches randomly combining libraries of vH and vL sequences in a single phage genome (vH and vL together are more than 200 amino acids), and Dower et al teach the larger fragments may still be effectively enriched by subsequent rounds of panning (see column 8) using the disclosed method. A person of ordinary skill in the art would have been motivated to use the method taught by Dower et al to obtain a specific binding pair member comprises an enzyme of 100-200 amino acids, because Dower et al teach that the disclosed method is useful to screen for enzymes and the method can be applied in therapeutic, diagnostic applications.

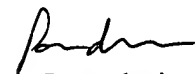
20. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday to Thursday from 6.30 AM to 4.00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith Macmillan, can be reached on (703) 308-4614. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0916.



P. Ponnaluri
Patent Examiner
Technology Center 1600
Art Unit 1627
8 April 2000.